

**WHAT IS CLAIMED:**

1. A method of monitoring one or more substances of interest comprising:  
applying a plurality of out-of-plane microneedles to a surface of an internal region, said  
microneedles long enough to sample one or more substances of interest at and/or just  
5 below said surface;  
said microneedles comprising one or more membranes on a side opposite a side applied to  
said surface such that said membrane is not placed under said surface;  
said membrane separating in said microneedles from a dialysis material;  
such that dialysis occurs outside of said internal region.
- 10 2. A method of monitoring one or more substances of interest comprising:  
applying a plurality of microneedles to a surface of an internal region while keeping one or  
more dialysis membranes and a dialysis fluid outside of said region thereby performing  
dialysis outside of said region.
3. The method of claim 2 or 1 further wherein:  
15 said one or more dialysis membranes comprise a large total membrane surface that can  
remain outside of said internal region.
4. The method of claim 2 or 1 further wherein:  
said surface is the skin of a mammal.
5. The method of claim 2 or 1 further wherein:  
20 said surface is the outer skin of a plant or part of a plant.
6. The method of claim 2 or 1 further wherein:  
said surface is a surface of a living organism or part or organ thereof.
7. The method of claim 2 or 1 further wherein:  
a plurality of said microneedles are pre-filled with a fluid before said applying.

8. A method of treating glucose disorders comprising:

applying a plurality of out-of-plane microneedles to the skin with a dialysis membrane remaining outside the skin thereby allowing for continuous glucose monitoring.

9. The method of claim 8 further comprising:

fixing a detecting substance useful in determining glucose levels on an opposite side of said dialysis membrane from said needles;

wherein said fixing is accomplished by placing a polymer-detecting substance solution at an opposite side of said membrane after higher temperature fabrication and/or assembly steps of said microneedles have been performed.

10. A device for monitoring a substance of interest comprising:

a group of out-of-plane microneedles;

a dialysis membrane proximal to a non-insertive side of said group;

a dialysis fluid in contact with a second surface of said dialysis membrane opposite said group ;

such that when said group is pressed against a surface of interest, said substance of interest within and/or behind said surface of interest can come in contact with a second surface of said dialysis membrane, allowing one or more substances of interest to pass into said dialysis fluid.

11. The device according to claim 10 further comprising:

one or more sensors in contact with said dialysis fluid for measuring and/or detecting one or more substances of interest.

12. The device according to claim 11 further comprising:

an area for holding calibration fluid; and

a valve between said calibration fluid and said dialysis fluid.

13. The device according to claim 10 further comprising:  
at least 8 microneedles in said group.

14. The device according to claim 10 further comprising:  
at least 50 microneedles in said group.

5 15. The device according to claim 10 further comprising:  
at least 200 microneedles in said group.

16. The device according to claim 10 further comprising:  
at least 750 microneedles in said group.

10 17. The device according to claim 10 further wherein:  
said dialysis membrane comprises one or more membranes, each membrane providing  
separation for a plurality of said microneedles.

18. The device according to claim 10 further wherein:  
said dialysis membrane comprises a plurality of membranes, at least some of said plurality  
of membranes providing separation for just one of said microneedles.

15 19. The device according to claim 10 further comprising:  
one or more sensors in contact with said dialysis fluid for measuring and/or detecting one  
or more substances of interest.

20. The device according to claim 10 further wherein:  
said microneedles are between about 100 micrometers and about 300 micrometers long.

20 21. The device according to claim 10 further wherein:  
said microneedles are between about 180 micrometers and about 220 micrometers long.

22. The device according to claim 10 further wherein:  
said microneedles are constructed of a metallic material.

23. The device according to claim 10 further wherein:

said microneedles are constructed of plastic.

24. The device according to claim 10 further wherein:

said microneedles are constructed of silicon.

25. The device according to claim 10 further wherein:

said microneedles are constructed of a semiconductor material.

26. The device according to claim 10 further wherein:

said membrane comprise a polymer and/or gel and/or porous poly-Si.

27. The device according to claim 10 further comprising:

one or more enzymes integrated into said membrane.

28. The device according to claim 10 further wherein:

a diffusion barrier and a check valve that are used as a two-way valve.

29. A method of in-device patterning of a temperature sensitive substance in an integrated system comprising:

performing one or more high temperature steps;

placing a solution of said temperature sensitive substance and a polymer in desired regions of said integrated system; and

gelling and/or immobilizing and/or polymerizing said solution in regions of interest using electromagnetic energy.

30. The method of claim 29 further comprising:

using a mask to define areas where said solution will not be immobilized and/or

polymerized and/or gelled; and

rinsing away remaining solution.

31. The method of claim 29 further wherein:

said temperature sensitive substance comprises:  
an enzyme.

32. The method of claim 29 further wherein:

5 said electromagnetic energy comprises UV light.

33. The method of claim 29 further wherein:

said polymerizing comprises crosslinking said polymer.

34. A method of constructing an integrated system including a temperature sensitive  
substance comprising:

10 performing one or more high temperature steps including a step of bonding a transparent or  
semi-transparent material on said system;  
placing a solution of said temperature sensitive substance and a polymer in desired regions  
of said integrated system such that said solution in part resides in areas between said  
transparent or semi-transparent material and other components of said system;  
15 hardening said solution in regions of interest using electromagnetic energy that can pass  
through said transparent or semi-transparent material; and  
rinsing unhardened portions of said solution.

35. The method of claim 34 further wherein:

said bonding is anodic bonding;

20 said hardening comprises crosslinking said polymer;

36. The method of claim 34 further wherein:

said polymer comprises PVA-SbQ;

said electromagnetic energy comprises UV light;

said UV light comprises light of about 365 nm or 900 mJ/cm<sup>2</sup>;

37. The method of claim 34 further wherein:

using a mask to define regions of said hardening;

such that said temperature sensitive substance becomes entrapped in locally formed gel regions; and

5 said rinsing comprises rinsing unlinked solution.

38. A method of monitoring one or more substances of interest comprising:

applying a plurality of out-of-plane microneedles to a surface of an internal region, said microneedles long enough to prestress a region of the surface at a needle lumen;

applying high pressure to a small local surface region through said microneedles to cause  
10 rupture of the cell matrix to open a connection between fluids inside the needle lumen and bodily fluids underneath the broken skin layer; and

using said connection to sample one or more substances of interest at and/or just below said surface.

39. A method of monitoring one or more substances of interest comprising:

15 applying a plurality of microneedles to a surface of an internal region while keeping one or more dialysis membranes and a dialysis fluid outside of said region thereby performing dialysis outside of said region.